

0607+001-02501

0607+001-02501

MKAVLLALLMAGLALQPGTALLCYSCKAQVSNEDCLQV
 ENCTQLGEQCWTARIRAVGLLTVISKGCSLNCVDDS
 QDYVYGKKNITCCDTLCLNASGAHALQAAAAIALLPAL
 GLLWGPGL

MKAVLLALLMAGLALQPGTALLCYSCAKVSNEDCLQV
 ENCTQLGEQCWTARIRAVGLLTVISKGCSLNCVDDS
 QDYVYGKKNITCCDIDLNCASGAHALQAAAAIALLPAL
 GLLWGPGL

FIG. 2

1 ATGAAGACAGT TTTT TTTATCCTGCTG G C C A C C T A C T T A G C C C T G C A T C C A G G T G C T G T
 -----+-----+-----+-----+-----+ 60
 T A C T T C T G T C A A A A A A A T A G G A C G A C C G G T G G A T G A A T C G G G A C T A G G T C C A C G A C G A

 M K T V F F I L L A T Y L A L H P G A A

 C T G C A G T G C T A T T C A T G C A C A G C A C A G A T G A A C A C A G A G A C T G T C T G A A T G T A C A G A A C
 61 -----+-----+-----+-----+-----+ 120
 G A C G T C A C G A T A A G T A C G T G C T G T C T A C T T G T T G T C T C T G A C A G A C T T A C A T G T C T T G

 L Q C Y S C T A Q M N N R D C L N V Q N

 T G C A G C C T G G A C C A G C A C A G T T G C T T T A C A T C G C G C A T C C G G G C C A T T G G A C T C G T G A C A
 121 -----+-----+-----+-----+-----+ 180
 A C G T C G G A C C T G G T C G T G T C A A C G A A A T G T A G C G C G T A G G C C C G G T A A C C T G A G A C A C T G T

 C S L D Q H S C F T S R I R A I G L V T

 G T T A T C A G T A A G G G C T G C A G C T C A C A G T G T G A G G A T G A C T C G G A G A A C T A C T A T T T G G G C
 181 -----+-----+-----+-----+-----+ 240
 C A A T A G T C A T T C C C G A C G T C G A G T G T C A C A C T C C T A C T G A G C C T C T T G A T G A T A A A C C C G

 V I S K G C S S Q C E D D S E N Y Y L G

 A A G A A G A A C A T C A C G T G C T G C T A C T C T G A C C T G T G C A A T G T C A A C G G G G C C C A C A C C C T G
 241 -----+-----+-----+-----+-----+ 300
 T T C T T C T T G T A G T G C A C G A C G A T G A G A C T G G A C A C G T T A C A G T T G C C C G G G T G T G G G A C

 K K N I T C C Y S D L C N V N G A H T L

 A A G C C A C C C A C C A C C C T G G G G C T G C T G A C C G T G C T C T G C A G C C T G T T G C T G T G G G C T C C
 301 -----+-----+-----+-----+-----+ 360
 T T C G G T G G G T G G T G G G A C C C G A C G A C T G G C A C G A G A C G T C G G A C A A C G A C A C C C G A G G

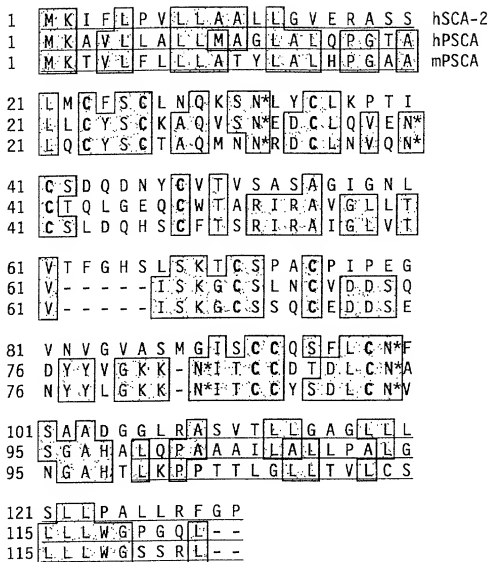
 K P P T T L G L L T V L C S L L L W G S

 A G C C G T C T G T A G G C T C T G G G A G A G C C T A C C A T A G C C C G A T T G T G A A G G G A T A G C T G C A C
 361 -----+-----+-----+-----+-----+ 420
 T C G G C A G A C A T C C G A G A C C C T C T C G G A T G G T A T C G G G C T A A C A C T T C C T A C T C G A C G T G

 S R L *

 T C C A C C C C A C C C C A C A C A G G
 421 -----+-----+ 441
 A G G T G G G G T G G G G T G T G T C C

FIG. 3



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FIG. 4

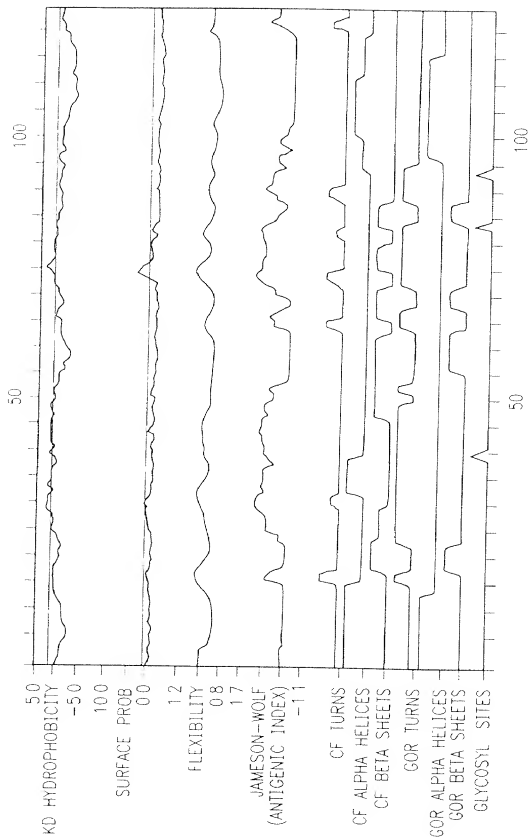




FIG. 5

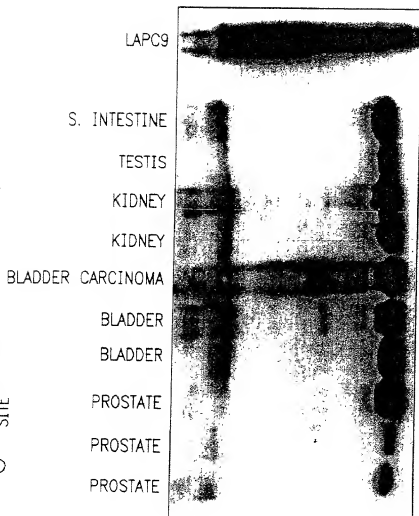


FIG. 6

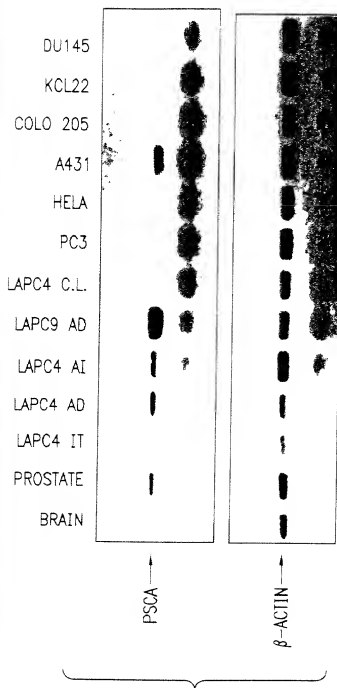
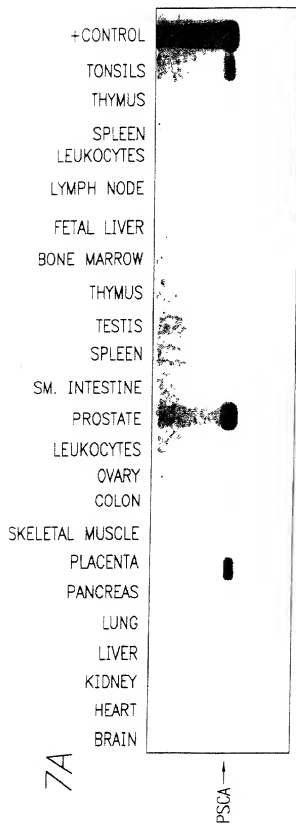


FIG. 8A

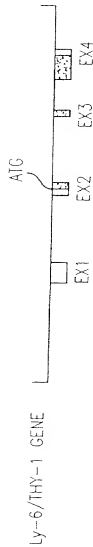


FIG. 8B

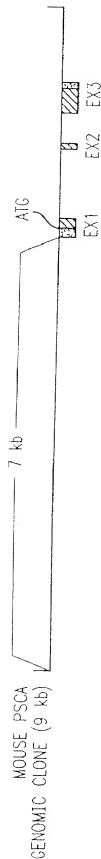


FIG. 8C



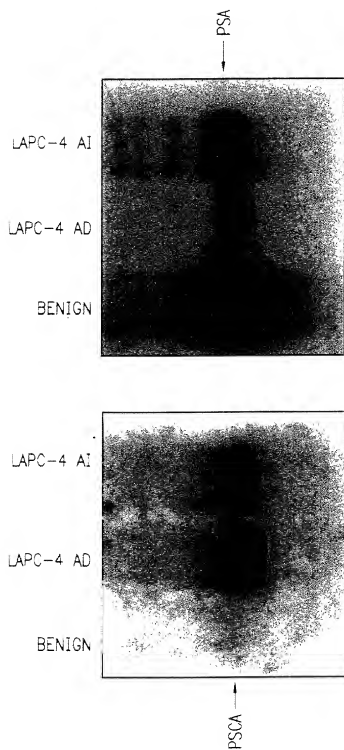


FIG. 9A

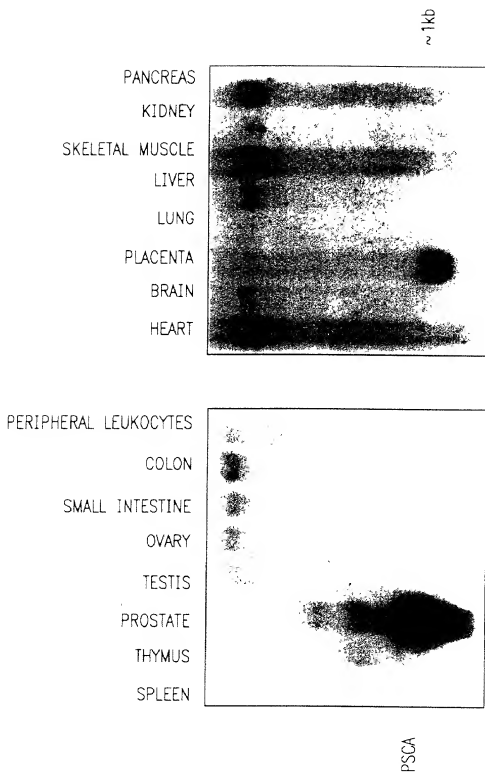


FIG. 9B

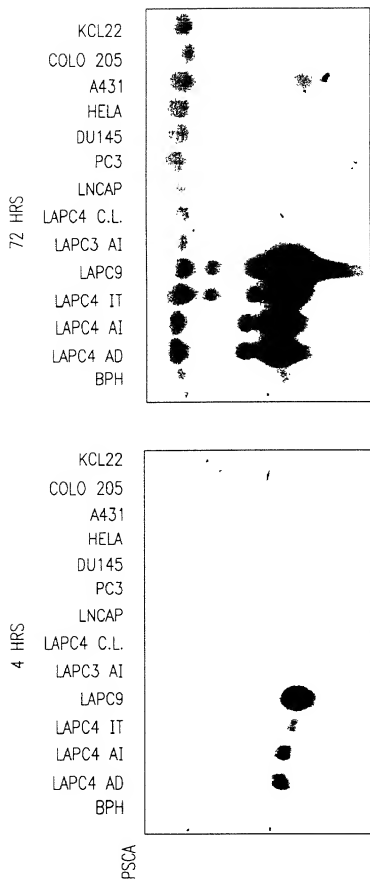


FIG. 10A

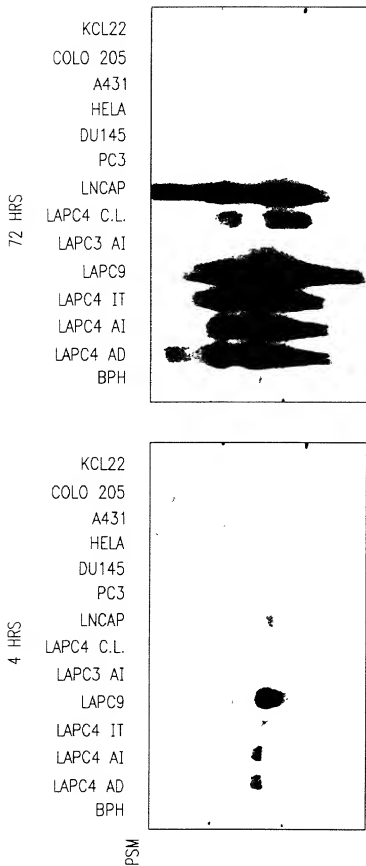
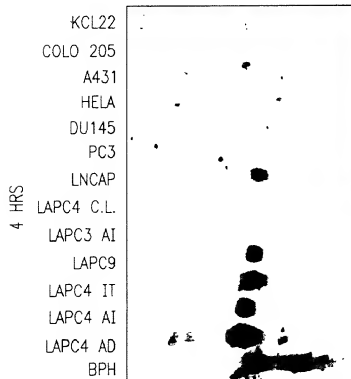
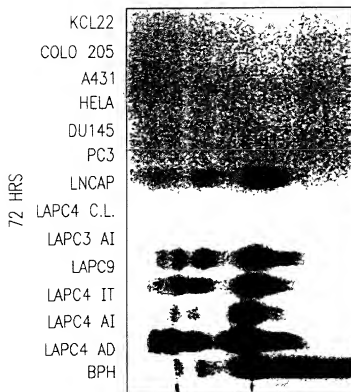


FIG. 10B



PSA

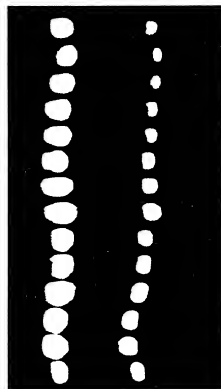


FIG. 10C

FIG. 11A

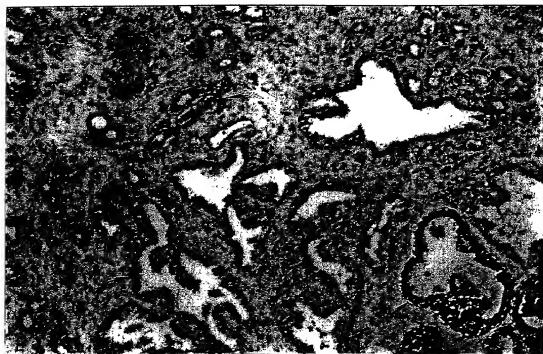
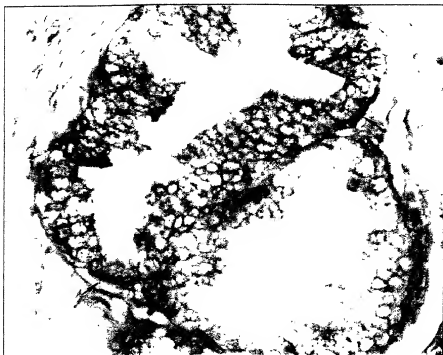


FIG. 11B

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09654811.072501



FIG. 11C

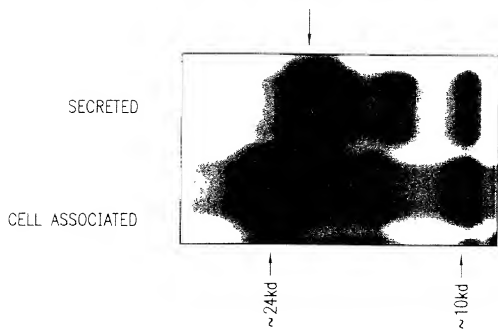
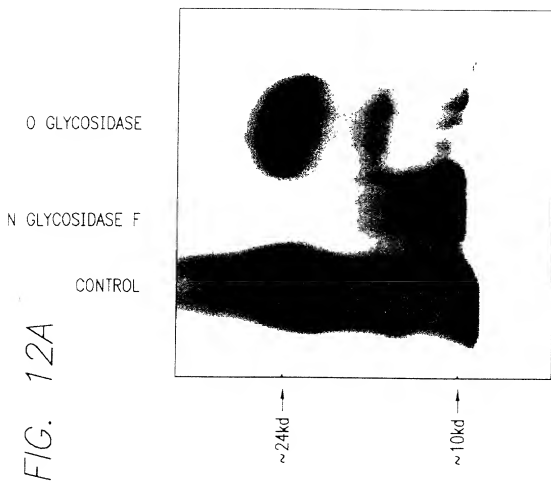


FIG. 12B

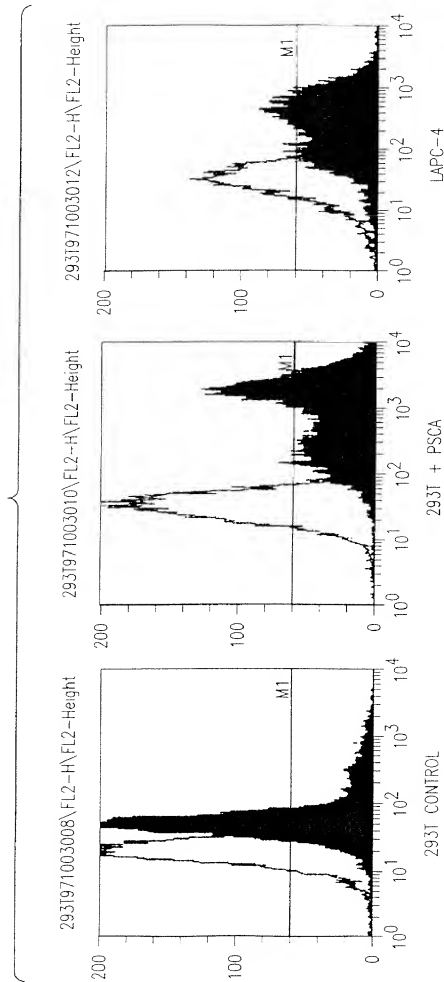


FIG. 12C

FIG. 13

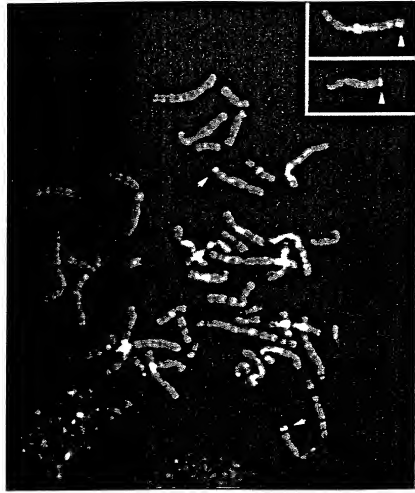


FIG. 14A

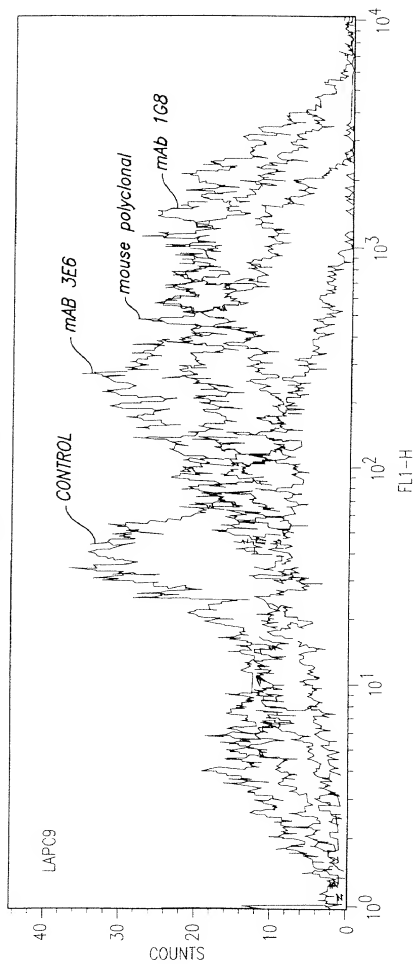


FIG. 14B

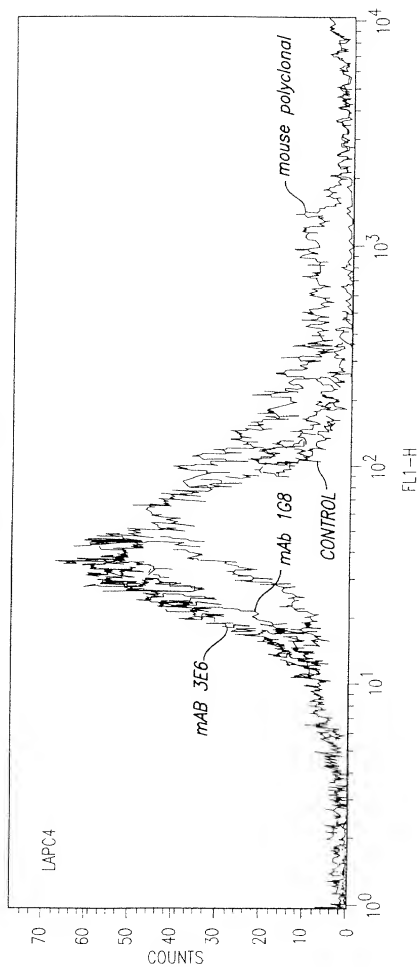


FIG. 14C

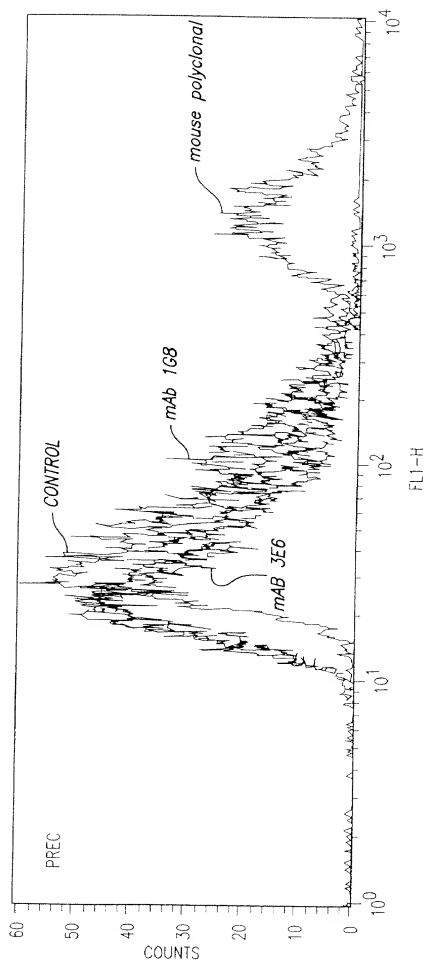


FIG. 15A

mAb	ISOTYPE	EPI TOPE MAP			
		FL (18-98)	N (2-50)	M (46-109)	C (85-123)
IgG1	k	2.039	0.007	0.628	0.000
2H9	k	1.318	0.863	0.032	0.021
3C5	k	2.893	1.965	0.016	0.005
3E6	k	0.328	0.024	0.069	0.370
4A10	k	2.039	1.315	0.000	0.014
2A2	k	1.366	0.733	0.010	0.003
3G3	k	2.805	1.731	0.004	0.000

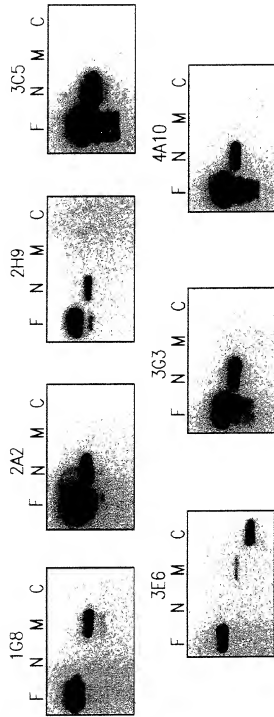


FIG. 15B

PROSTATE STEM CELL ANTIGEN (PSCA) IS A GPI-ANCHORED PROTEIN

1	M	K	I	F	L	P	V	L	A	A	L	G	V	E	R	A	S	hSCA-2
1	M	K	A	V	L	L	A	L	M	A	G	L	A	L	Q	P	G	hPSCA
1	M	K	I	V	L	F	L	L	A	T	Y	A	L	H	P	C	A	mPSCA
21	L	M	C	F	S	C	L	N	Q	K	S	N	L	Y	C	L	K	P
21	L	L	C	Y	S	C	K	A	D	V	S	N	L	D	C	L	Q	V
21	L	L	C	Y	S	C	T	A	Q	M	N	N	R	D	C	L	N	Y
41	G	S	D	Q	D	N	Y	C	V	T	V	S	A	S	A	G	I	G
41	G	T	Q	L	G	E	Q	C	W	T	A	R	T	R	A	V	D	L
41	G	S	L	D	Q	H	S	C	F	I	S	R	I	R	A	I	G	L
61	V	T	F	G	H	S	L	S	K	I	C	S	P	A	C	P	I	P
61	V	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
61	V	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
81	V	N	V	G	V	A	S	M	C	T	S	C	C	Q	S	F	F	C
76	D	Y	V	G	K	K	-	N	I	T	C	G	D	T	D	E	C	N
76	N	Y	L	G	K	K	-	N	I	T	C	C	Y	S	D	L	C	N
101	S	A	A	D	G	G	L	R	A	S	V	I	T	L	G	A	G	L
95	S	G	A	H	A	I	Q	P	A	A	I	L	A	L	P	A	L	G
95	N	G	A	A	T	L	K	P	T	T	L	G	L	T	V	C	S	
121	S	L	P	A	L	L	R	F	G	P	-	-	-	-	-	-	-	-
115	L	L	W	C	P	G	Q	N	-	-	-	-	-	-	-	-	-	-
115	L	L	W	C	S	S	R	L	-	-	-	-	-	-	-	-	-	-

FIG. 16A

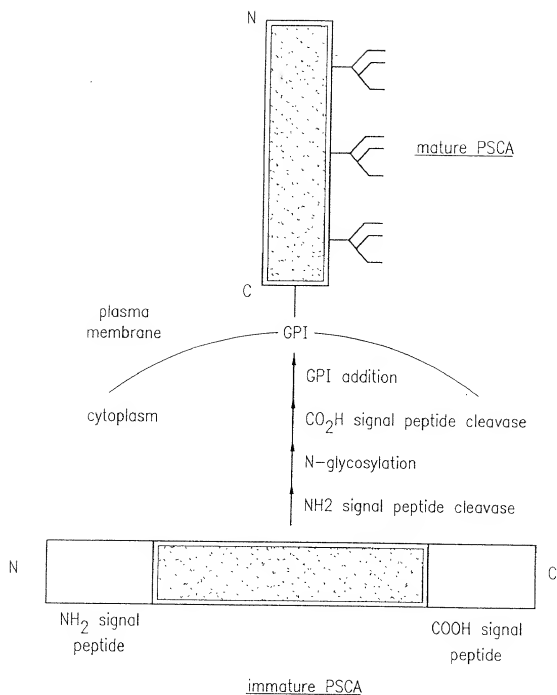


FIG. 16B

FIG. 17

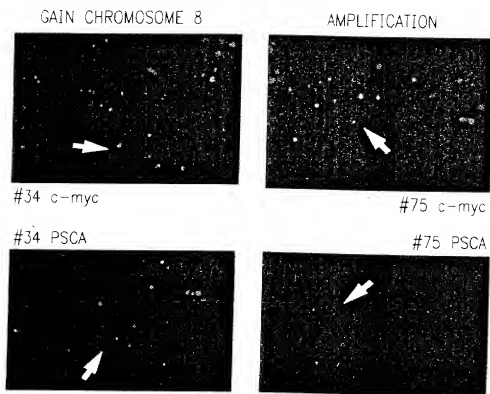
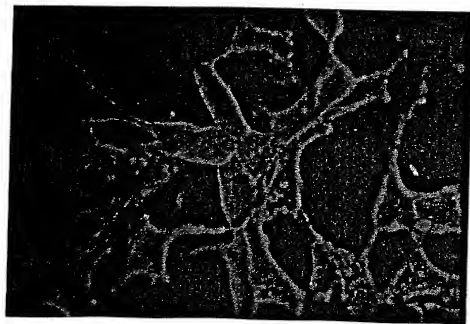


FIG. 18



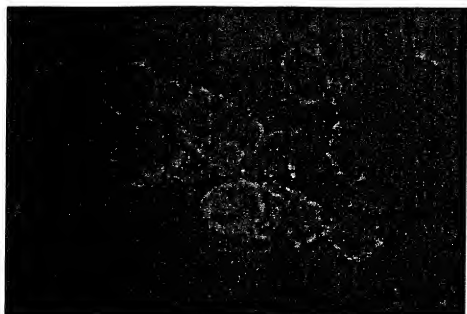


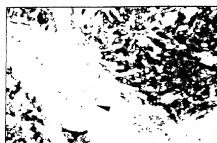
FIG. 19

FIG. 20

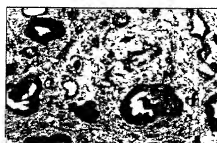


FIG. 21

PSCA IMMUNOSTAINING OF PRIMARY TUMORS



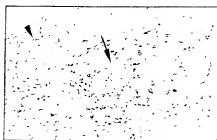
patient 1:mAb 1G8



patient 2:mAb 1G8

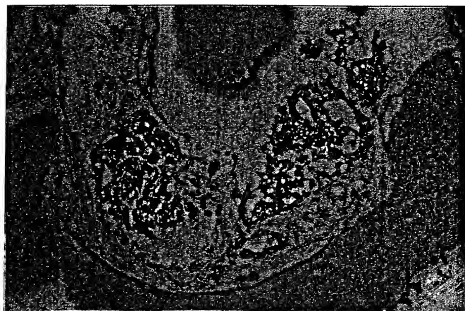


patient 3:mAb 1G8



patient 4:mAb 3E6

FIG. 22



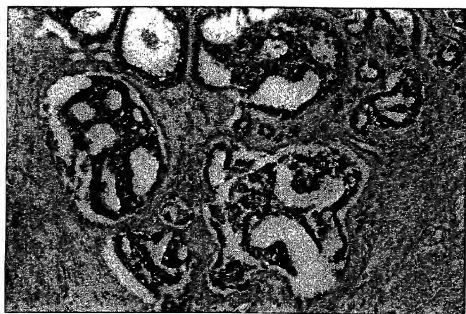


FIG. 23

FIG. 24



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FIG. 25

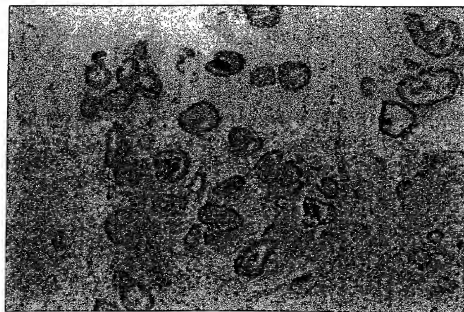
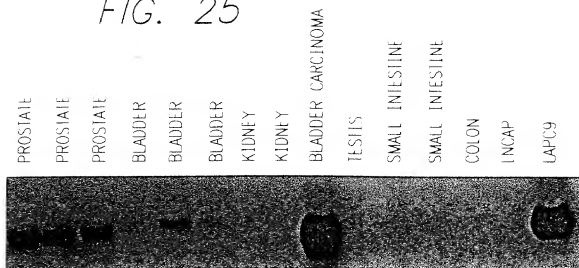


FIG. 26

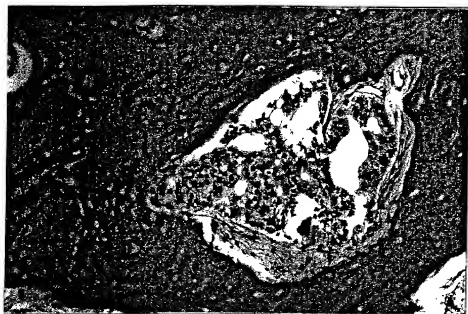
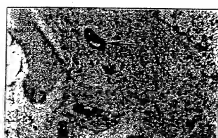
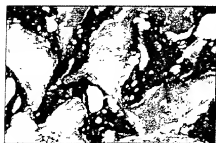


FIG. 27



Patient 5: H and E
and mAb 1G8



Patient 4: H and E
and mAb 3E6

FIG. 28

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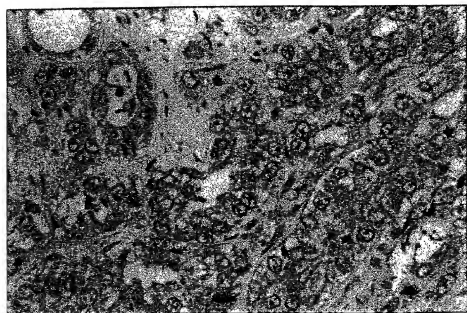
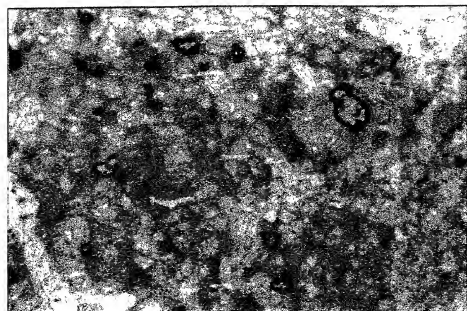


FIG. 29

FIG. 30



09854811-072501

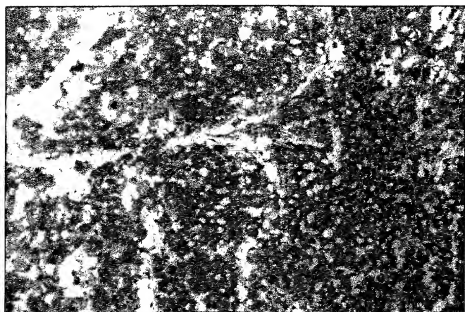


FIG. 31

FIG. 32

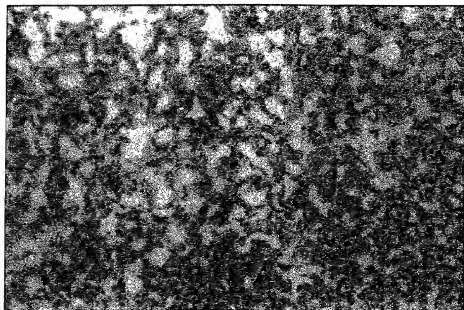
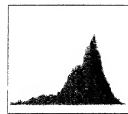
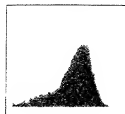
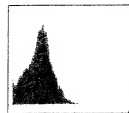


FIG. 33

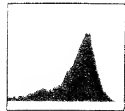
SECONDARY ANTIBODY



4A10



3C5



3E6

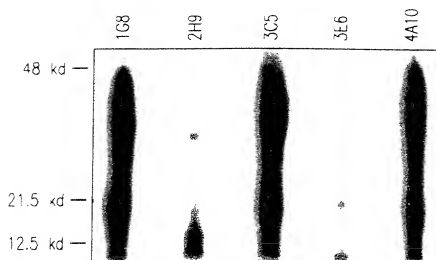


FIG. 34

FIG. 35

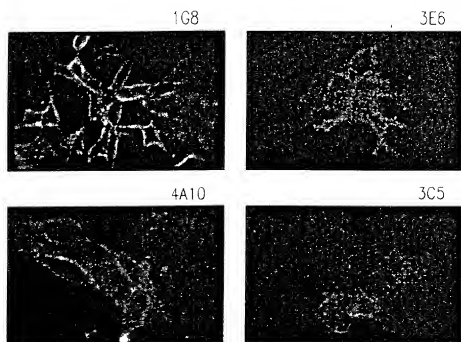


FIG. 36

105220-11845860

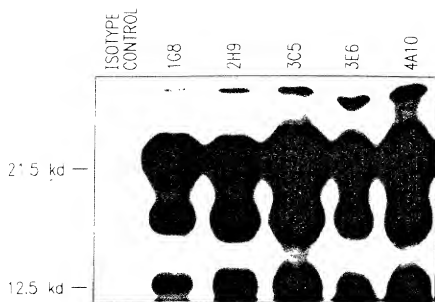
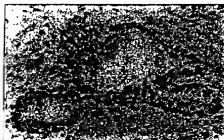


FIG. 37

NORMAL: ISOTYPE CONTROL



NORMAL: PSCA mAb 3E6



NORMAL: PSCA mAb 1G8

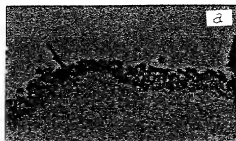


ATROPHY: PSCA mAb 2H9



FIG. 38

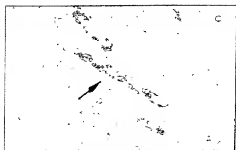
FIG. 39A



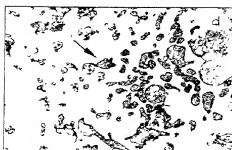
BLADDER: 1G8



COLON: 1G8



KIDNEY: 3E6



PLACENTA: 3E6

PROSTATE

PROSTATE

PROSTATE

KIDNEY

KIDNEY

KIDNEY

BLADDER

BLADDER

BLADDER

LAPC 9



PSCA



ACTIN

FIG. 39B

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FIG. 40A

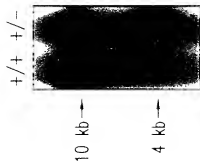
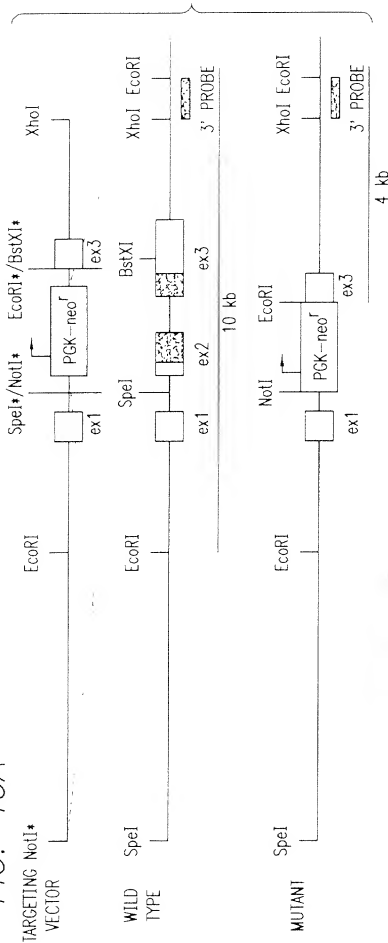


FIG. 40B

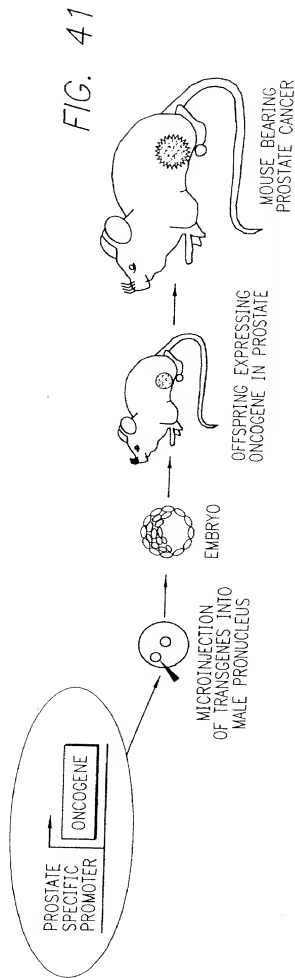


FIG. 41

TRANSGENE	TARGET TISSUES	CHARACTERISTICS
C3(1) (-3 kb)/ SV40 LARGE+SMALL, T MAROULAKOU et al. 1994 PNAS	PROSTATE (SECRETORY CELLS) URETHRAL, MAMMARY AND SWEAT GLAND	LOW-GRADE PIN 8-12 WKS HIGH-GRADE PIN 8-12 WKS INVASIVE CARCINOMA 28 WKS NO METASTASES
PROBASTIN (-426 bp)/ SV40 LARGE+SMALL, T GREENBERG et al. 1995 PNAS	PROSTATE (SECRETORY CELLS)	LOW-GRADE PIN 5-8 WKS HIGH-GRADE PIN 8-12 WKS INVASIVE CARCINOMA 12 WKS METASTASES IN LYMPH NODE, LUNG, LIVER AND BONE
CRYPTDIN2 (-6.5 kb)/ SV40 LARGE+SMALL, T GARABEDIAN et al. 1998 PNAS	PROSTATE (NEUROENDOCRINE CELLS) SMALL INTESTINE	LOW-GRADE PIN 8-12 WKS HIGH-GRADE PIN 8-12 WKS INVASIVE CARCINOMA 16 WKS METASTASES IN LYMPH NODE, LUNG, LIVER, AND BONE

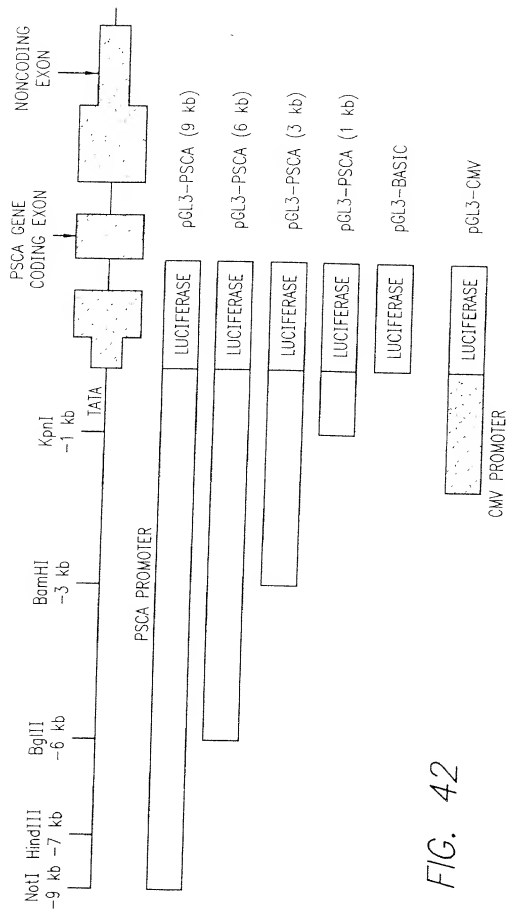


FIG. 42

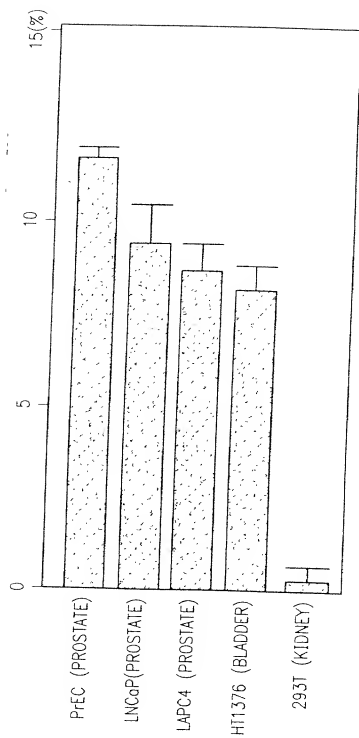


FIG. 43

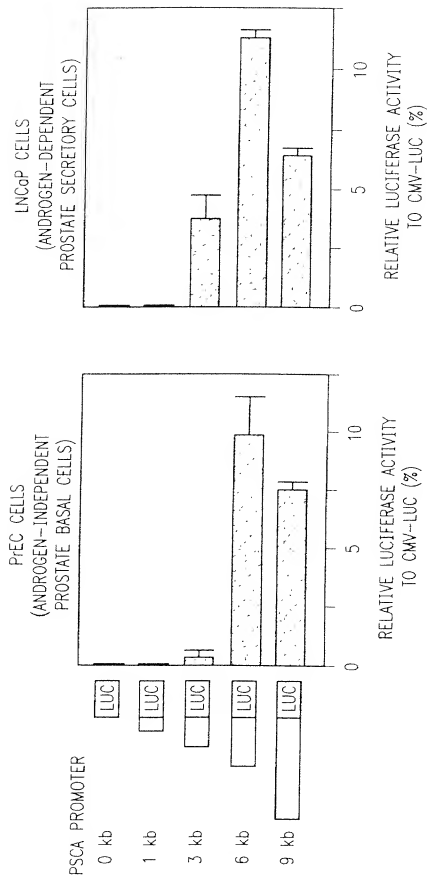
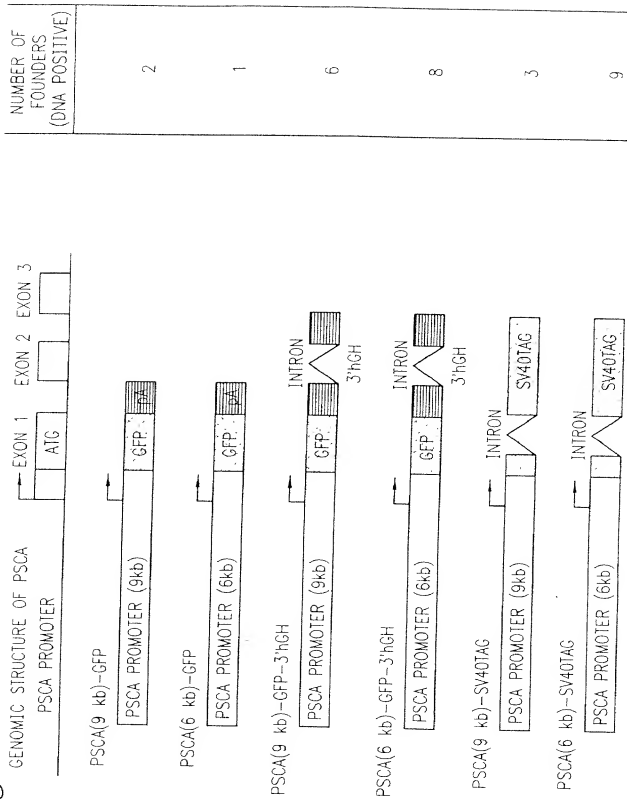


FIG. 44

FIG. 45



NEGATIVE TISSUES

STOMACH

SMALL INTESTINE

COLON

SEMINAL VESICLE

URETHRA

TESTIS

LIVER

KIDNEY

LUNG

BRAIN

HEART

SKELETAL MUSCLE

OVARY

UTERUS

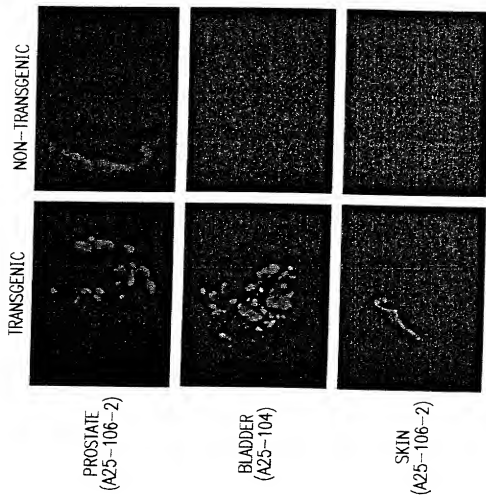
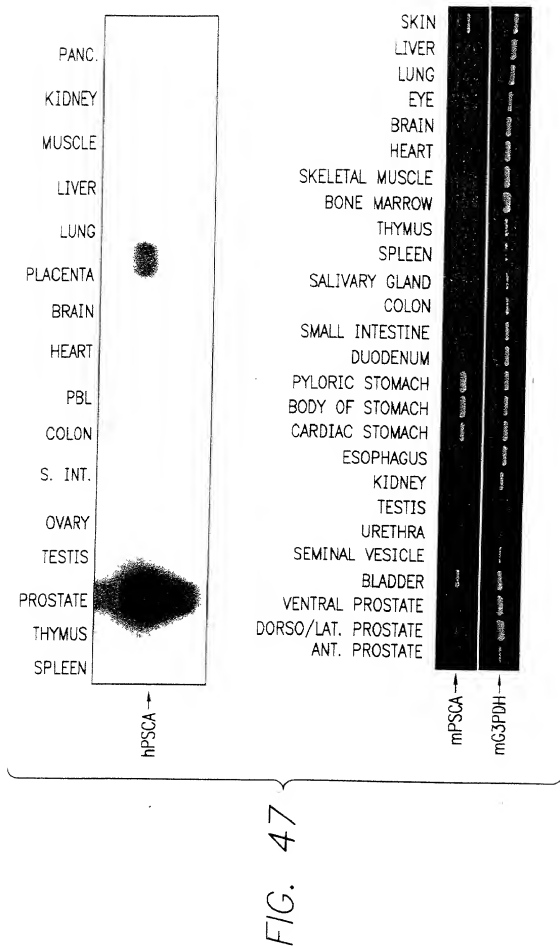


FIG. 46



COLEMAN

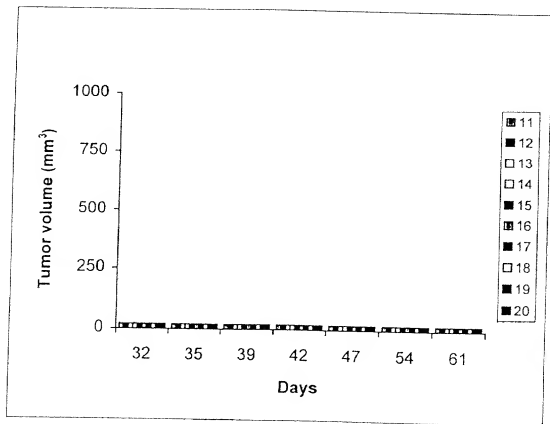
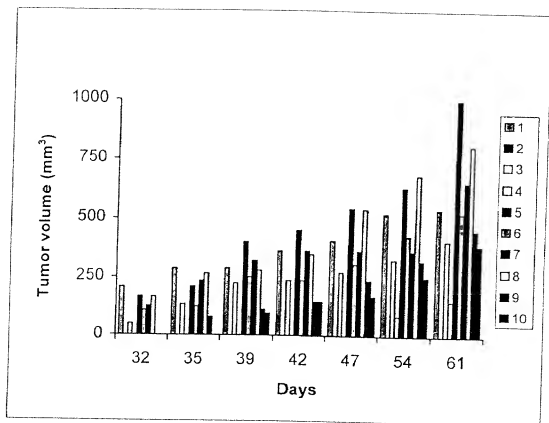


FIG. 49

A

Epitope recognized (OD 450 nm)

mAb	Isotype	F (18-98)	N (2-50)	M (46-109)	C (85-123)
1G8	IgG1 k	1.485	0.004	1.273	0.003
2A2	IgG2a k	0.973	0.631	0.023	0.010
2H9	IgG1 k	1.069	1.026	0.002	0.001
3C5	IgG2a k	1.916	1.709	0.006	0.002
3E6	IgG3 k	1.609	0.036	1.133	2.118
3G3	IgG2a k	2.805	1.731	0.004	0.000
4A10	IgG2a k	1.053	0.493	0.000	0.001

B

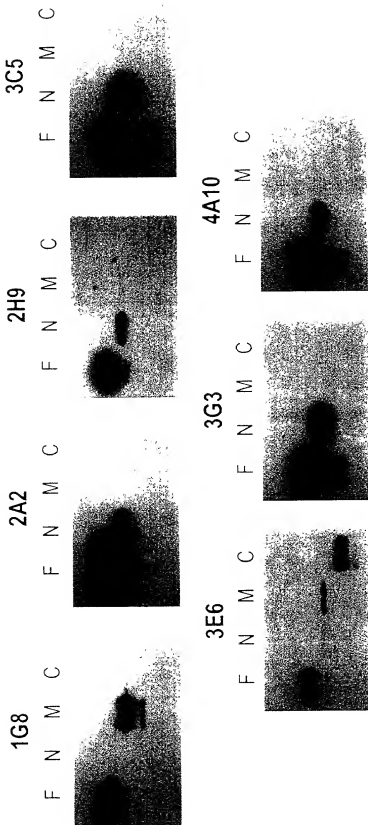
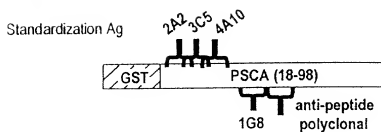
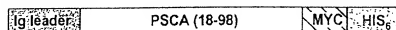


FIG. 50

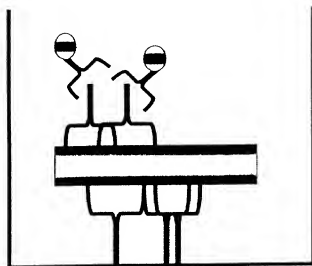
A



Engineered mammalian secreted form



B



Anti-IgG2a HRP

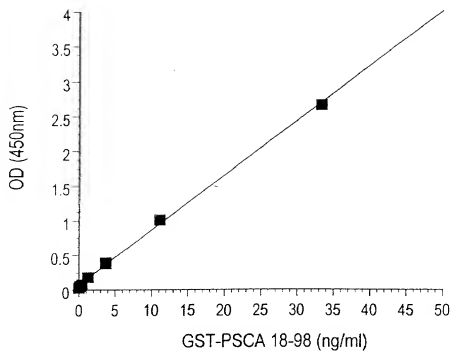
Anti-PSCA mAbs 3C5+4A10+2A2 (IgG2a)

PSCA

Affinity purified anti-peptide polyclonal
+ mAb 1G8 (IgG1)

FIG. 51

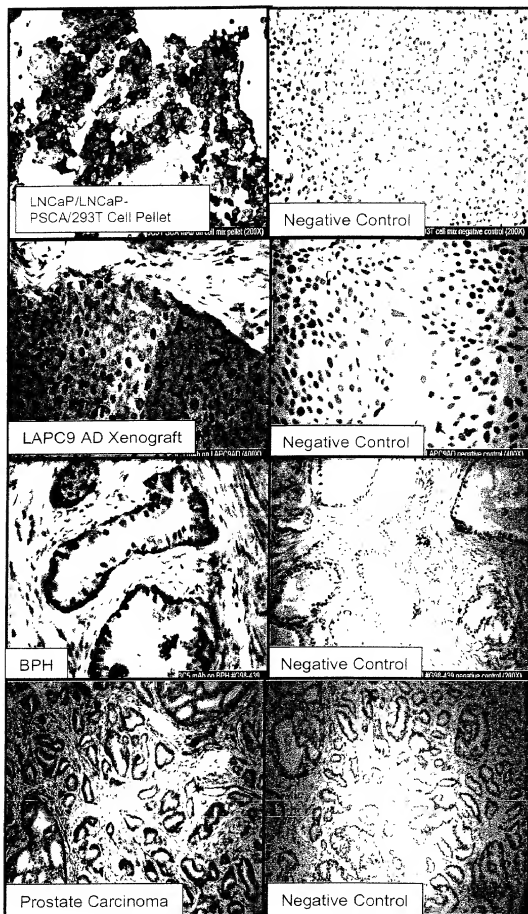
A



B

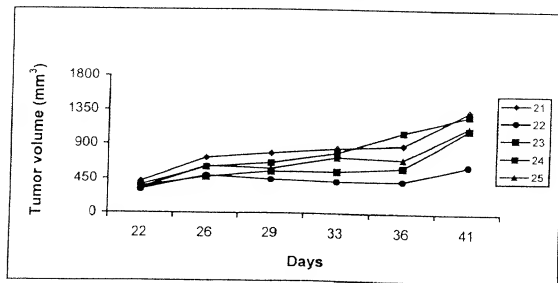
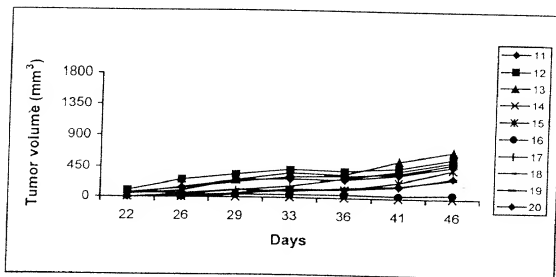
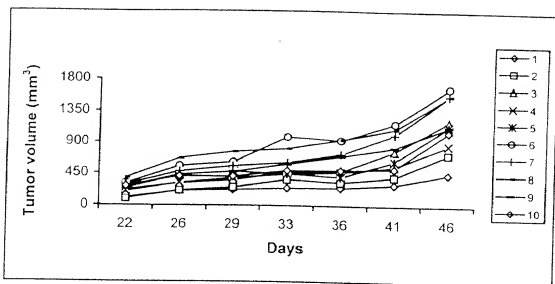
Sample	OD+range (n=2)	ng/ml
vector	0.005+0.001	ND
vector+hu serum	0.004+0.001	ND
secPSCA	2.695+0.031	32.92
secPSCA+hu serum	2.187+0.029	26.55

FIG. 52



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FIG. 53



0054811.072501

FIG. 54

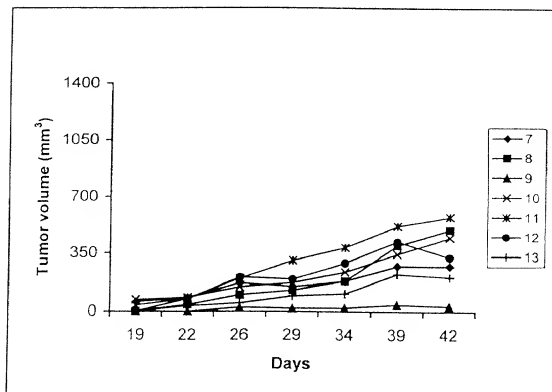
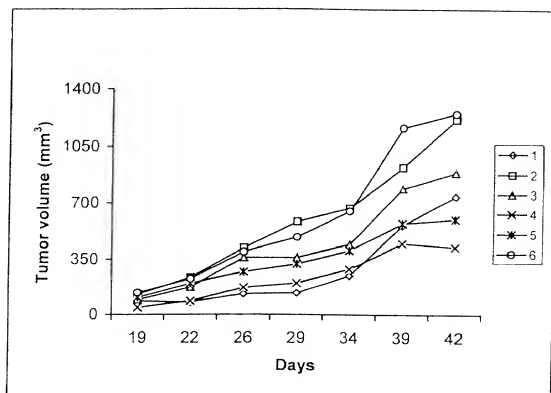
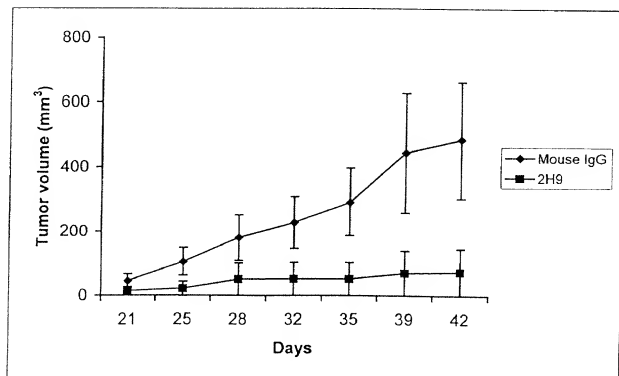
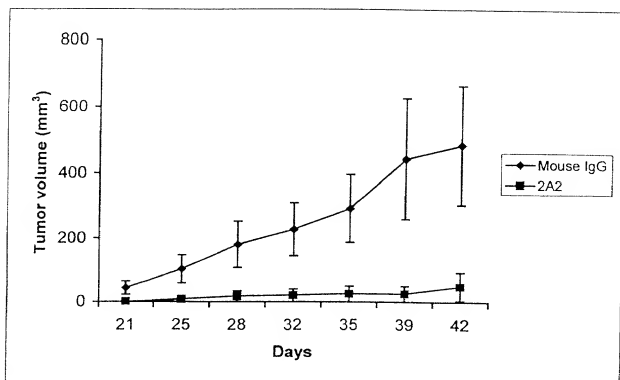


FIG. 55



105220.1184560

FIG. 56

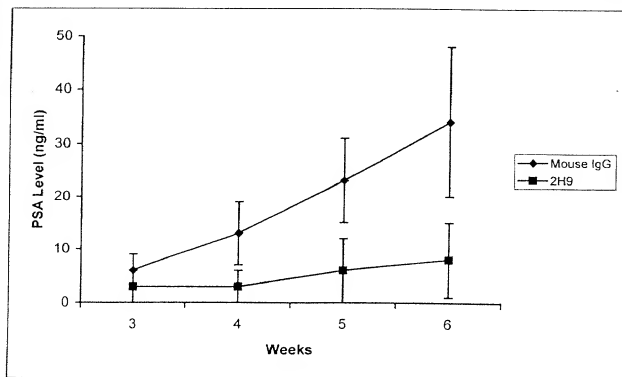
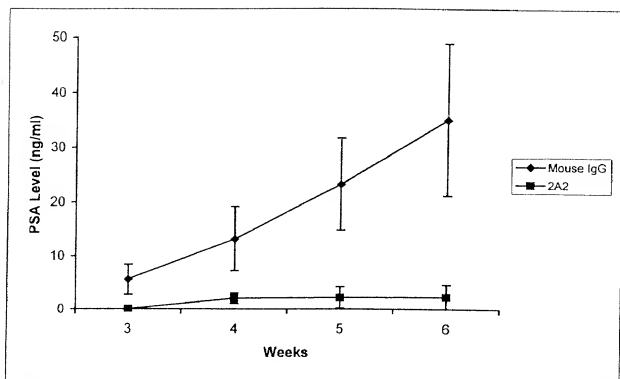


FIG. 57

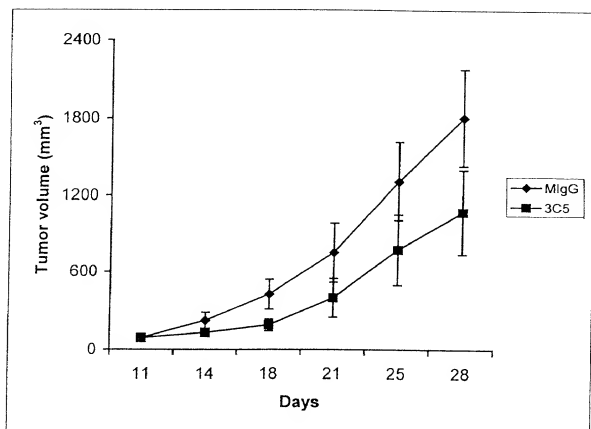


FIG. 58

TGCTTCTTCCTGATGGCAGTGGTTATAGAGTCAATTGAGAGTTTCAGCTGCAGCAGTCT 60
C F L M A V V I G V N S E V Q L Q Q S 20

GGGCGAGAACTTGTGAGGTCAGGGCCCTCAGTCAAGTTGTCTCTGCACAGCTTCTGGCTTC 120
G A E L V R S G A S V K L S C T A S G F 40

----- CDR1 -----
AACATTAAAGACTCTATATACACTGGGTGAATCAGAGGCCTGACCCAGGGCCTGGAGTGG 180
N I K D Y Y I H W V N Q R P D Q G L E W 60

----- CDR2 -----
ATTGGATGGATTGATCCTGAGAATGGTGACACTGAATTGTCCCGAAGTTCAGGGCAAG 240
I G W I D P E N G D T E F V P K F Q G K 80

GCCACTATGACTGCAGACATTTTCTCCAACACAGCCTACCTGCACCTCAGCAGCCTGACA 300
A T M T A D I F S N T A Y L H L S S L T 100

TCTGAAGACACTGCGTCTATTACTGTAAACGGGGGTTTCTGGGGCCCAAGGGACTCTG 360
S E D T A V Y Y C K T G G F W G Q G T L 120
----- CDR3 -----

GTCACTGTCTCTGCAGCCAAACGACACCCCATCTGTCTATCCACTG
V T V S A A K T T P P S V Y P L

FIG. 59

TTGGTAGCAACAGCCTCAGATGCCACTCCAGGTCCAACCTGCAGCAACCTGGGTCTGAA 60
L V A T A S D V H S Q V Q L Q Q P G S E 20

CTGGTAGGCCCTGGAACTTCAGTGAAGCTGTCTGCAAGGCTTCTGGCTATACATCTCC 120
L V R P G T S V K L S C K A S G Y T F S 40
CDR1

AGCTACTGATGCACCTGGGTGAAGCAGAGCCTGGACAAGGCCTTCAGTGGATTGGAAAT 180
S Y W M H W V K Q R P G G L E W I G N 60

ATTGACCCCTGGTAGTGGTTACACTAACTACGCTGAGAACCTCAAGACCAAGGCCACACTG 240
I D P G S G Y T N Y A E N L K T K A T L 80
CDR2

ACTGTAGACACATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGACATCTGAGGAC 300
T V D T S S S T A Y M Q L S S L T S E D 100

TCTGCAGTCTATTACTGTACACCGCATCTACTATGATTACGACGGGATTTGCTTACTG 360
S A V Y Y C T S R S T M I T T G F A Y W 120
CDR3

GGCCAGGAGACTCTGGTCACTGTCTCTGCACTACACACACAGCCCATCTGTCTATCCA 420
G Q G T L V T V S A A T T A P S V Y P 160

CTGGCC
L A

FIG. 60

AATGACTCGGGTTGAGCTGGGTTTTTATTATTGTTCTTTTAAAGGGTCCGAGTGAA 60
 N D F G L S W V F I I V L L K G V R S E 20

GTGAGGCTTGAGGAGCTCTGGAGGCTGGGTGCAACCTGGAGGATCCATGAATCTCC 120
 V R L E E S G G G W V Q P G G S M K L S 40

TGTGTAGCCTCTGGATTTACTTTCACTAATTACTGGATGACTTGGTCCGCCAGTCTCCA 180
 C V A S G F T F S N Y W M T W V R Q S P 60
 CDR1

GAGAAGGGGCTTGAGTGGGTTGCTGAAATTCGATTGAGATCTGAAATATGCAACACAT 240
 E K G L E W V A E I R L R S E N Y A T H 80
 CDR2

TATCGGAGTCTGTGAAGGGAATTCACCATCTCAAGAGATGATCCAGAAGTCGTCTC 300
 Y A E S V K G K F T I S R D D S R S R L 100

TACTTGCAATGACAACACTTAAGACCTGAAGACAGTGGAAATTTATTACTGTACAGATGGT 360
 Y L Q M N N L R P E D S G I Y Y C T D G 120

CTGGACGACCTAATCTGGGGCAAGGAGCTGTGGTCACTGTCTCTGCAGCCAAACGACA 420
 L G R P N W G Q G T L V T V S A A K T T 140
 CDR3

CCCCACTCTGTCTATCCACTGGCCCTTGTTGTA
 P P S V Y P L A P C V

FIG. 61

CDR1 Comparisons

1G8	1gG _{1k}	Middle	G	F	N	I	K	D	Y	Y	I	H
2H9	1gG _{1k}	N-Term.	G	F	T	F	S	N	Y	W	M	T
4A10	1gG _{2ak}	N-Term.	G	Y	T	F	S	S	Y	W	M	H

CDR2 Comparisons

1G8	1gG _{1k}	W	I	D	P	E	N	G	D	T	E	F	V	P	K	F	Q	G		
2H9	1gG _{1k}	E	I	R	L	R	S	E	N	Y	A	T	H	Y	A	E	S	V	K	G
4A10	1gG _{2ak}	N	I	D	P	G	S	G	Y	T	N			Y	A	E	N	L	K	T

CDR3 Comparisons

1G8	1gG _{1k}	G	G	F														
2H9	1gG _{1k}	L	G	R	P	N												
4A10	1gG _{2ak}	R	S	T	M	I	T	T	G	F	A	Y						

038441-02201

FIG. 62

A



B



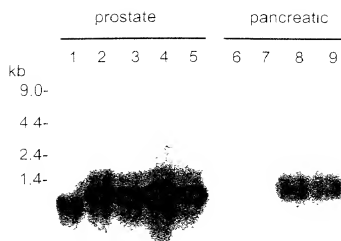
C



D



FIG. 63



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FIG. 64

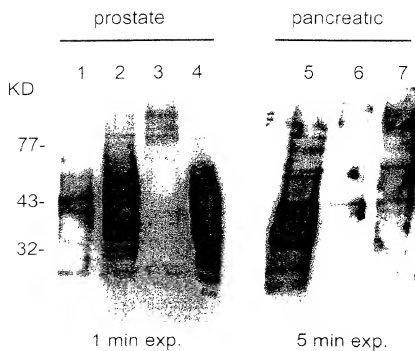


FIG. 65

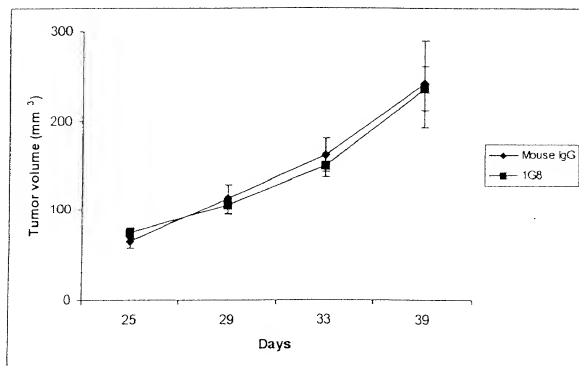
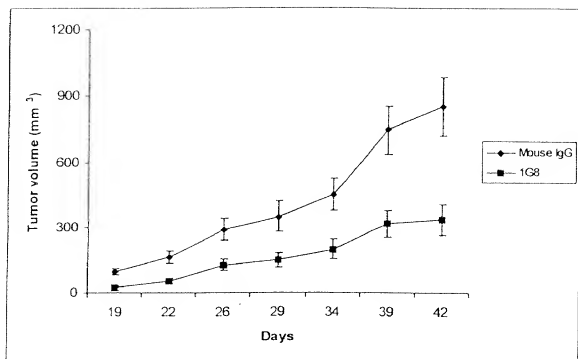
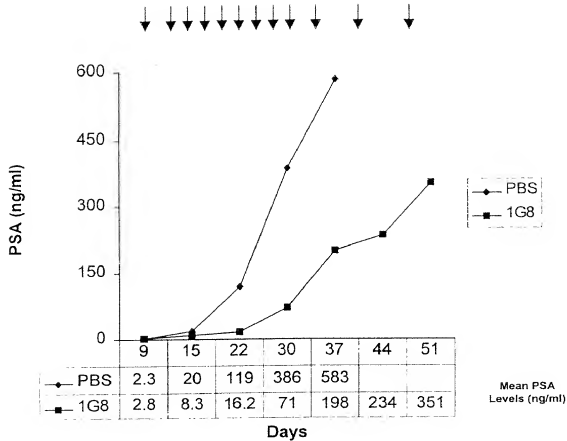


FIG. 66

A)



B)

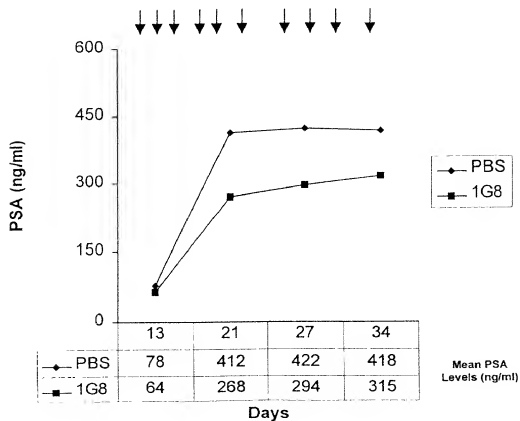
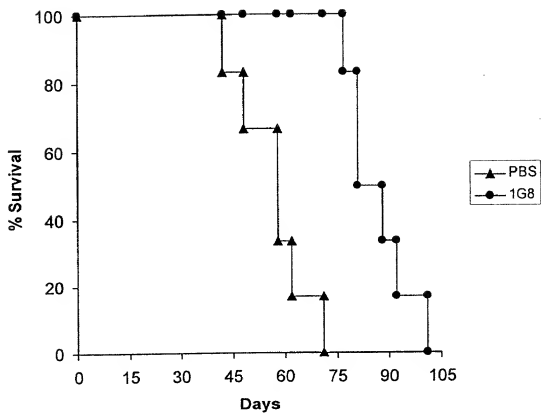
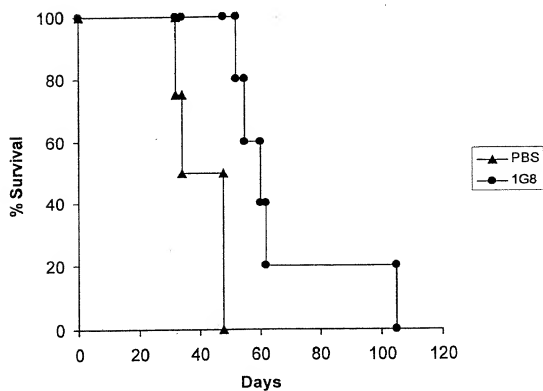


FIG. 67

A)



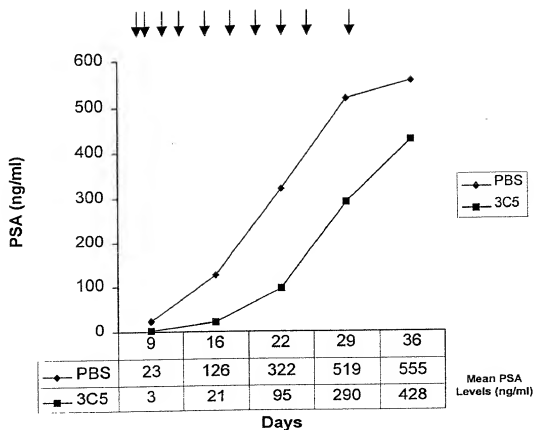
B)



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FIG. 68

A)



B)

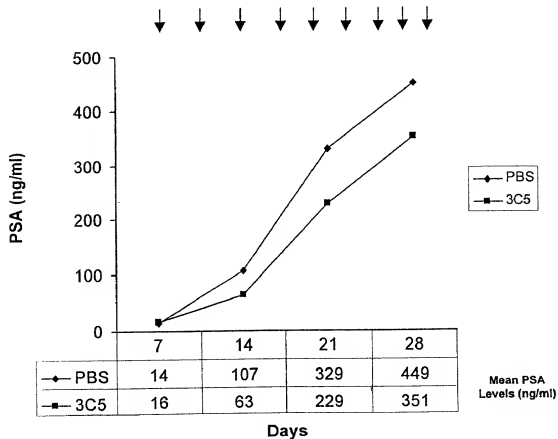
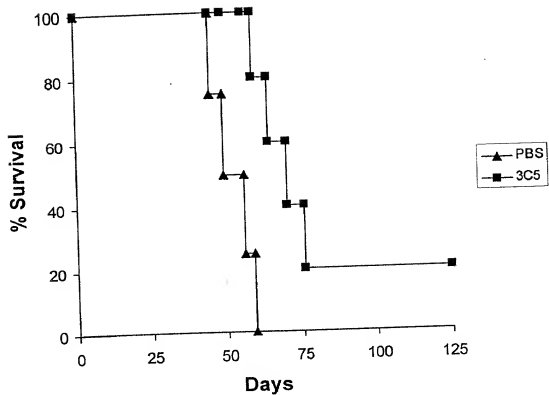


FIG. 69

A)



B)

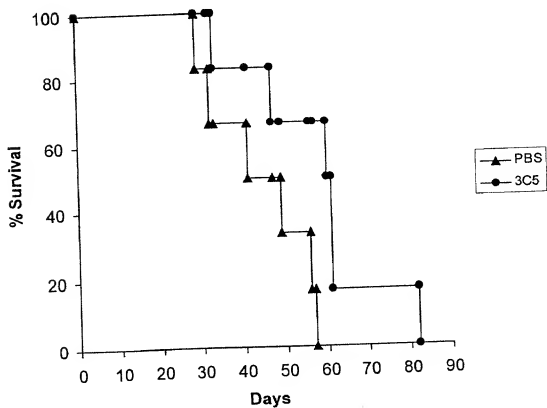


FIG. 70

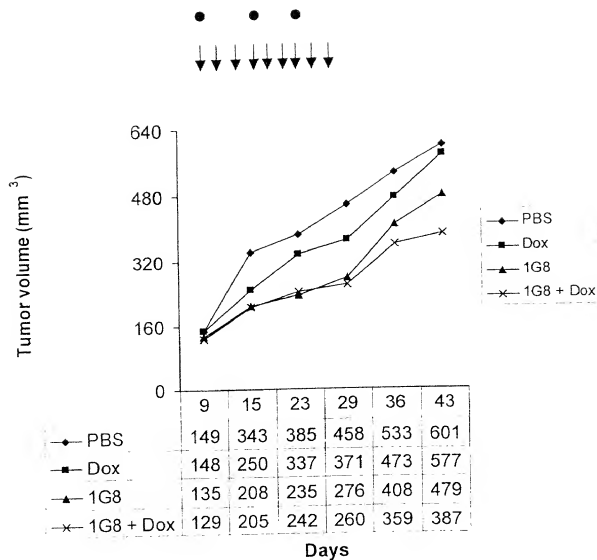
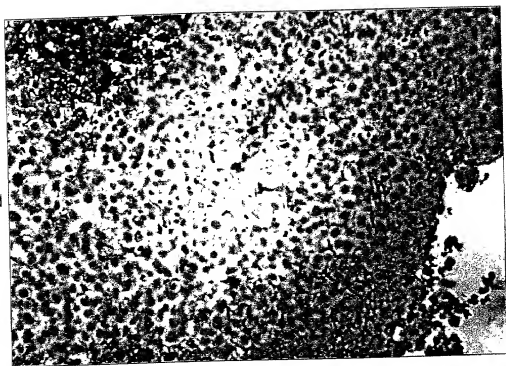
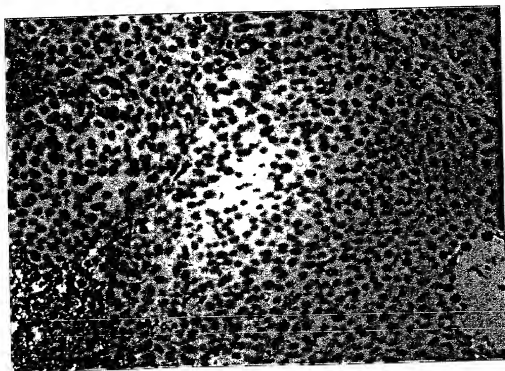


FIG. 71

3C5 Treated



mIgG Treated



00851811-072511

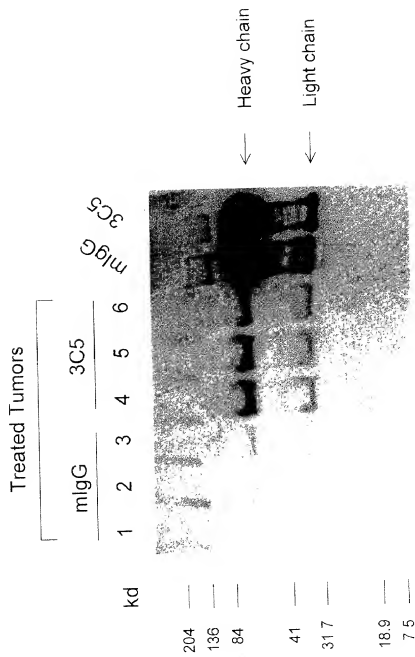


FIG. 72

105220*11845860

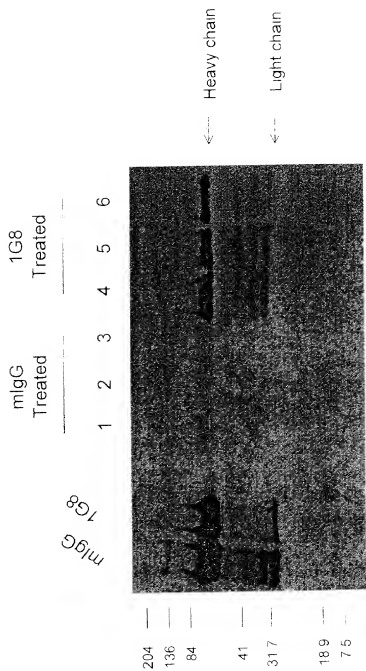


FIG. 73